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     FILE 'CAPLUS' ENTERED AT 14:40:03 ON 14 NOV 2004
L5             0 S L4 FULL
L6         67741 S DIMETHYLAMINO
L7         14784 S L6 AND PHENYL
L8           564 S L7 AND PROPIONIC
L9           537 S L7 AND PROPIONIC ACID
L10          254 S L9 AND ETHYL ESTER
L11            1 S L9 AND ETHYLESTER
L12          352 S L9 AND ETHYL AND ESTER
L13          240 S L12 AND PY<1999
L14           57 S L13 AND CARBOXYLIC ACID
L15           15 S CYCLOHEXENE AND L14

=> d 1-15 l15 ibib abs hitstr

L15  ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1990:77858  CAPLUS
DOCUMENT NUMBER:          112:77858
TITLE:                    Preparation of chartreusin derivatives as anticancer
                          agents
INVENTOR(S):              Yamada, Shuitsu; Sugi, Hideo; Kon, Kenji
PATENT ASSIGNEE(S):       Ishihara Sangyo Kaisha, Ltd., Japan
SOURCE:                   Jpn. Kokai Tokkyo Koho, 96 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     JP 62099391           A2    19870508    JP 1985-238525           19851024 <--
     JP 06033311           B4    19940502
PRIORITY APPLN. INFO.:                       JP 1985-238525           19851024
GI
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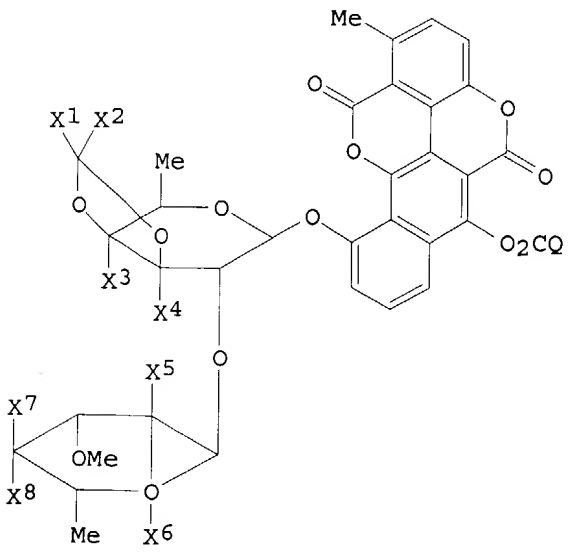

I

AB The title compds. [I; X1 = H, (un)substituted C1-3 alkyl; X2 = (un)substituted C1-3 alkyl, C1-2 alkylcarbonyl-C1-2 alkyl, Ph, **phenyl**-C1-2 alkyl, furyl, thienyl; X1X2 = (un)substituted C3-7 cycloalkylidene; provided that X1 = X2 = C≤4 alkyl, or when X2 = (un)substituted Ph, phenylalkyl, furyl, thienyl, X1 = H; X3, X4 = H, Me; when X3 = Me, X4 = H; X5 = H, OH, NH2; X6 = H, OH; X5X6 = O; when X5 = OH,

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Uploading C:\STNEXP4\QUERIES\383c.str

L1 STRUCTURE UPLOADED

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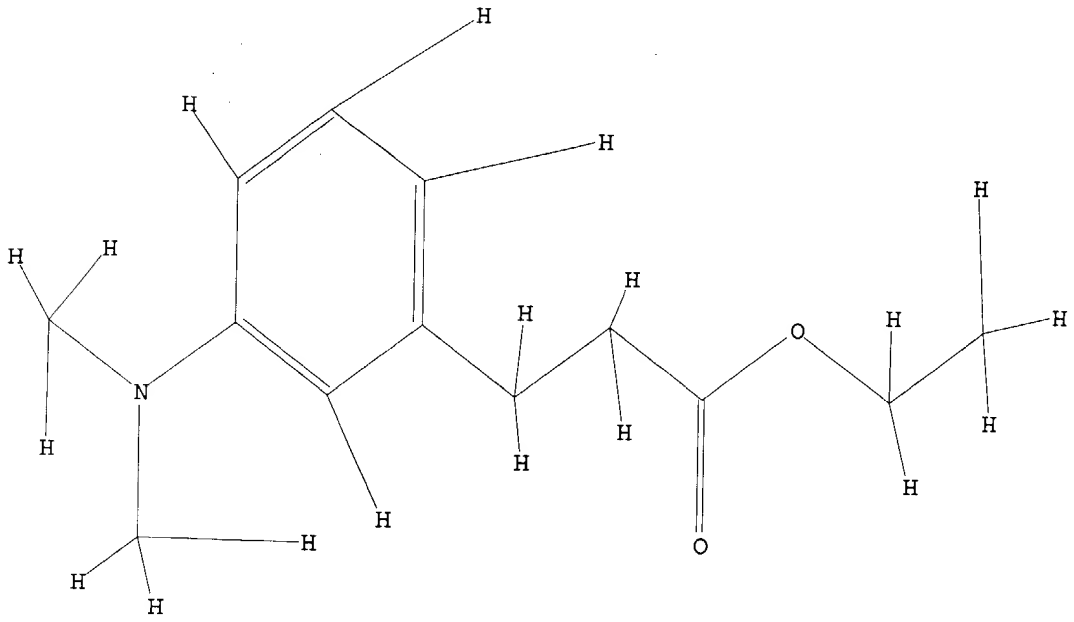
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 14:39:29 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 93666 TO ITERATE

1.1% PROCESSED 1000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **INCOMPLETE**
PROJECTED ITERATIONS: EXCEEDS 1000000
PROJECTED ANSWERS: EXCEEDS 0

L2 0 SEA SSS SAM L1

L3 0 L2

=> s l1 full
REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 14:39:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - >1,000,000 TO ITERATE

< 21.3% PROCESSED 400000 ITERATIONS 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.06

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **INCOMPLETE**
PROJECTED ITERATIONS: EXCEEDS 1000000
PROJECTED ANSWERS: EXCEEDS 1

L4 1 SEA SSS FUL L1

L5 0 L4

NH2, X6 = H; X7 = H, NH2; X8 = H, OH; when X7 = NH2, X8 = H; Q = (un)substituted C1-11 alkyl, C2-11 alkenyl, C3-11 alkynyl, C3-10 cycloalkyl, C3-10 cycloalkenyl, C1-10 alkylcarbonyl, etc.], which show excellent anticancer activity when administered to a part of the body other than that where the cancer is located, are prepared Thus, N-carbobenzoxy-L-proline was added to a solution of 3',4'-O-isopropylidene-2'',4''-bis(tert-butyldimethylsilyl)chartreusin, followed by SOCl2 at 0°, and the mixture was stirred 1 h at 0° to give 6-O-(N-carbobenzoxyprolyl)-3',4'-O-isopropylidene-2'',4''-bis(tert-butyldimethylsilyl)chartreusin, which was treated with 3N aqueous HCl in THF to give 6-O-(N-carbobenzoxyprolyl)chartresusin. Approx. 440 I were prepared Most them were tested against mouse leukemia P388 in mice and, at 10-160 mg/kg/day on the 1st, 5th and 9th days or at 20 or 40 mg/kg/day on the 1st and 5th day after the cancer inoculation, extended the life span by 127-286%.

L15 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1964:425111 CAPLUS
DOCUMENT NUMBER: 61:25111
ORIGINAL REFERENCE NO.: 61:4256c-h,4257a-h,4258a-c
TITLE: Basic substituted esters of arylalkylcarboxylic acids and related compounds
AUTHOR(S): Wollweber, H.; Hiltmann, R.
CORPORATE SOURCE: Farbenfabriken Bayer A.-G., Wuppertal-Elberfeld, Germany
SOURCE: Med. Chem. Abhandl. Med.-Chem. Forschungsstaetten Farbwerke Hoechst. A.G. (**1963**), 7, 150-70
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB Basic derivs. of hydracylic and phenylglycolic esters were prepared for pharmacol. testing (Kreiskott, et al., ibid. 117). The Grignard reagent from 171 g. nortricyclyl bromide and 26 g. Mg in 700 mL. Et2O was treated with 105 g. PhCN, the mixture refluxed overnight and treated with dilute HCl, the aqueous layer heated 2 h. at 80° and extracted with Et2O, and the extract distilled to give 67 g. Ph nortricyclyl ketone, b6 150°. Similarly prepared were RCOR1 (I) (R, R1, b.p./mm., and m.p. given): Ph, bicyclo[2.2.1]-5-hepten-2-yl, 138°/6, - (semicarbazone m. 163-4°); Ph, cycloheptyl, 120°/0.1, -; Ph, cyclopentyl, 130°/8, -; Ph, 6-methylbicyclo[2.2.1]-5-hepten-2-yl, 114°/1, 82-3°; Ph, Et2CH, 78°/0.3, -; 3-cyclohexen-1-yl, Me2CH, 90°/12, -. To a solution of 164 g. iso-PrCOCl in 360 mL. petr. ether was added 142 g. AlCl3 and then 138 g. veratrole dropwise at -5°. The mixture was stirred overnight, treated with ice and HCl, and steam distilled The non-volatile residue was extracted with Et2O and the extract distilled to give 66 g. 3,4-(MeO)2C6H3COCHMe2, b10 165-70°. Similarly prepared were I (R1 = iso-Pr), (R and b.p./mm. given): 4-MeOC6H4, 130°/6; 4-EtOC6H4, 133°/2; 4-ClC6H4, 110°/7; 4-MeC6H4, 100°/8; 4-EtC6H4, 105°/2; 5,2-Me(MeO)C6H3, 114°/6; 2,5-ClMeC6H3, 126°/6; 2-thienyl, 88°/7. A mixture of 33 g. 1,2-(CH2O)C6H4 and 88 g. (iso-PrCO)2O was saturated at -5-0° with BF3, poured into a solution of 200 g. NaOAc in 600 mL. water, and extracted with Et2O to give 46.7 g. 3,4-(CH2O2)C6H3COCHMe2 (II), b0.1 104. A solution of 44 g. BCH:CH2 in 200 mL. Et2O was treated dropwise at 10-20° with 23 g. cyclopentadiene, refluxed 2 h., and distilled to give 39.3 g. endo-bicyclo[2.2.1]-5-hepten-2-yl Ph ketone, b0.1 115°; semicarbazone m. 174°. Similarly prepared were I (R = Ph) (R1 and m.p. given): 6-carboxybicyclo[2.2.1]-5-hepten-2-yl, 130-2; 1,2-dimethyl-4-carboxy-5-cyclohexen-1-yl, 137. To a solution of 300 g. K2Cr2O7 and 250 g. H2SO4 in 1500 mL. water was added at 30° during 1 h. 207 g. 3,4-(CH2O2)C6H3CH(OH)Pr-iso, b0.6 118-20°. The mixture was heated 1 min. at 52°, cooled, saturated with Na2SO4, and extracted with Et2O to give 150 g. II. To 217 g. activated Zn dust in a mixture of 200 mL. each of THF and benzene was added with heating and stirring 30 g. BrCH2CO2Et (III) and 25 g. PhCOCPr-iso (IV). After the reaction had begun a mixture of 510 g. III, 342 g. IV, and 300 mL. of each solvent was added slowly, and the mixture refluxed 1 h., treated with aqueous NH4Cl, and extracted with Et2O to give 485 g. PhC(OH)(Pr-iso)CH2CO2Et (V), b0.7 102-5°. A mixture of 485 g. V, 90 g. KOH, 500 mL. MeOH, and 500 mL. water was

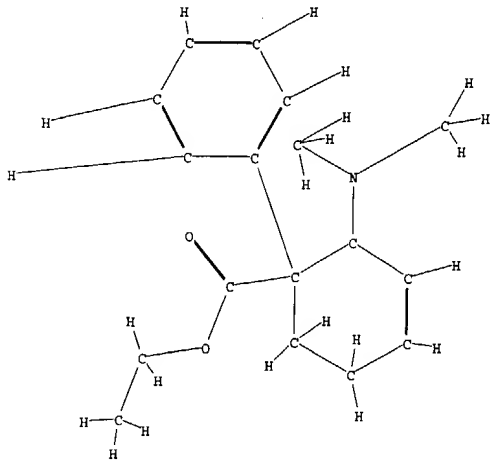
refluxed 2 h., the MeOH distilled, and the aqueous solution extracted with Et2O and acidified to precipitate 365 g. PhC(OH)(Pr-iso)CH2CO2H (VI), m. 118-19° (EtOAc). A mixture of 17g. VI, 15g. Et2NCH2CH2Cl, and 150 mL. iso-PrOH was refluxed 6 h., evaporated in vacuo, treated with aqueous K2CO3, extracted with Et2O, and distilled to give 18.5g. PhC(OH)(Pr-iso)CH2CO2CH2CH2NEt2, b0.1 144°; HCl salt (VII) m. 112-14°. Similarly prepared were the following R1R2C(OH)(CH2)nCO2R3 (VIII) (n = 1) [R1, R2, b.p./mm. of **ester** (R3 = Et), m.p. free acid (R3 = H), R3, b.p./mm. of basic **ester**, and m.p. of basic **ester** citrate (or HCl) salt given]: Ph, bicyclo[2.2.1]-5-hepten-2-yl, 140°/0.2, 156°, CH2CH2NEt2 (Z), 190°/0.3, [82-5°, CH2CH2Q (Q = morpholino), 200°/0.5, -, CH2CH2X (X = piperidino), 210°/0.1, -]; Ph, bicyclo[2.2.1]-hept-2-yl, -, -, Z, 190°/0.3, 103-4°; Ph, 6-methylbicyclo[2.2.1]-5-hepten-2-yl, -, -, Z, 210°/0.3, 83-5°; Ph, nortricyclyl, 140°/0.1, -, Z, 190°/0.1, 92-3°; Ph, cyclohexyl, -, 172°, Z, 184°/0.1, [134-5°], [(CH2)3NMe2 170°/0.5, 113-15°, CH2CH2X, 210°/0.3, -]; Ph, Ph, -, 215° (decomposition), Z, -, 123-4°; Ph, 1-cyclohexen-1-yl, -, 155-6°, Z, 190°/0.4,-; Ph, 3-cyclohexen-1-yl,-, 156, Z, 220°/0.2, 120°; Ph, cycloheptyl, -,110-11°, Z, 184°/0.1, 88-9°; Ph, cyclopentyl,-, 135-6°, Z, 190°/1, 104-5°; Ph, cyclopropyl, -, 107-8°, Z, 150°/0.1, 137°; Ph, Et, -, 134-5°, Z, 150/0.1°, 78-80°; Ph, vinyl, 104°/0.6,-, Z, 150°/0.1, 76; Ph, Pr,-, 123-4°, Z, 154°/0.3, 85-7; Ph, Bu, 118°/0.2, 109-10°, Z, 154°/0.2, 92-3; Ph, iso-Bu, 114°/0.2,-, Z, 170°/0.5, 65; Ph, CHMeEt, 110°/0.2, 83-5°, Z, 150°/0.2, 102-4°; Ph, tert-Bu, 100°/0.2, 141-2°, Z, 146°/0.1, 100-2°; Ph, CHEt2, 110°/0.3, 95-6°, Z, 168°/0.2, 99-100°; PhCH2CH2, Me, 125°/0.1, -, Z, 165°/0.3, 87-8°; Ph, CMe:CH2, 115°/1.5, 124-5°, Z, 156°/0.5, 102-3° (HCl salt); 4-MeOC6H4, iso-Pr, , 115°, Z, 175°/0.2, 85-7°, [CH2CH2Y (Y = pyrrolidino), 180°/0.5, 69-70°]; 4-EtOC6H4, iso-Pr, -, 115-16°, Z, 180°/0.3, 89°; 3,4-(MeO)2C6H3, iso-Pr, -, 113-14°, Z, 190°/0.3, 98-9°; 3,4-(CH2O2)C6H3, iso-Pr,-, 137-8°, Z, 186°/0.5, 84-6°; 4-EtC6H4, iso-Pr, -, 102-3°, Z, 145°/0.2, 86-7°; 4-MeC6H4, iso-Pr, 110°/0.4, 119°, Z, 164°/1, 85-6° (HClsalt); 5,2-Me(MeO)C6H3, iso-Pr,-,-, Z, 165°/0.3, 93-5°; 2,5-ClMeC6H3, CHMe2, -, -, Z, 165°/0.8, 90°; 4-ClC6H4, iso-Pr, -, 99°, Z, 162°/0.3, 81°; 3-cyclohexen-1-yl, iso-Pr, -, -, Z, 165°/0.6, 94-5°; 2-thienyl, CHMe2, 98°/0.2, 116-17°, Z, 154°/0.3, 87°. Prepared from VI were the following VIII (R1 = Ph, R2 = iso-Pr, n = 1) [R3, b.p./mm., and m.p. citrate (or HCl) salt given]: CH2CH2NMe2, 128°/0.3, 74-5°; (CH2)3NMe2, 140°/0.3, 63-5°; (CH2)3NEt2, 164°/0.3, 77-8°; CHMeCH2NMe2, 134°/0.6, 104-5° (HCl salt); CH2CMe2NMe2, 128°/0.8, 98-9° (HCl salt); CH2CMe2CH2NEt2, 150°/0.4, 111-12° (HCl salt); CH2CH2Y, 158°/0.3, 124-5° (HCl salt); (CH2)3Y, 161°/0.3, 107-8°; CHMeCH2Y, 162°/0.6, 78-80°; CH2CH2X, 160°/0.4, 122-3° (HCl salt); CH2CH2Q, 176°/0.4, 125-6° (HCl salt); a, 180°/0.3, -; b, 170°/0.6, 124-6° (HCl salt). A Grignard solution from 320 g. iso-PrBr, 62 g. Mg, and 1200 mL. Et2O was added at -5° to a solution of 391 g. BzCO2Et (IX) in 1000 mL. Et2O, the mixture stirred 6 h. at 20°, hydrolyzed with aqueous NH4Cl, and extracted with Et2O to give 327 g. VIII (R1 = Ph, R2 = iso-Pr, R3 = Et, n = 0), b0.4 84-6°,hydrolyzed to 210g. free acid, m. 145-6°. Substituted benzoylformic esters were reduced by iso-PrMgBr to the corresponding mandelic esters. Thus, 192 g. 4-MeC6H4COCO2Et with the Grignard reagent from 160 g. iso-PrBr gave 173 g. 4-MeC6H4CH(OH)CO2Et, b0.5 94°, m. 76-7°, hydrolyzed to 135 g. acid, m. 145-6°. A solution of 48 g. iso-PrCOCO2Et in 300 mL. Et2O was treated with the Grignard reagent from 82.6 g. 3-ClC6H4Br, 11 g. Mg, and 250 mL. Et2O to give 50.7 g. VIII (R1 = 3-ClC6H4, R2 = iso-Pr, R3 = Et, n = 0), b1 120°; corresponding acid m. 105-7° (AcOEt). Prepared were

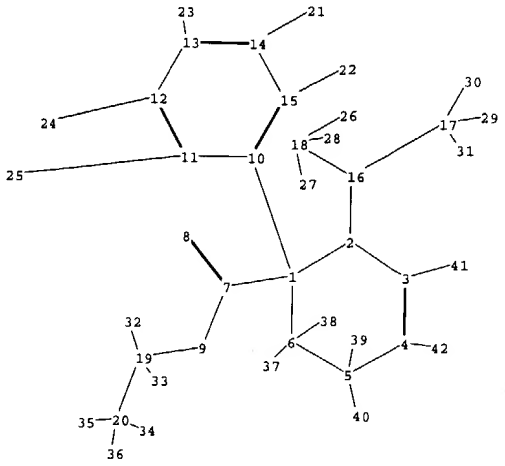
VIII (R1 = Ph, R2 = iso-Pr, n = 0), [R3, b.p./mm., and m .p. HCl salt (or citrate) salt given]: Z, 128°/0.3, 106-7° (citrate); CH2CH2NMe2, 120°/0.3, 183-4°; (CH2)3NMe2, 132°/0.5, 141-2°; CHMeCH2NMe2, 120°/0.5, 150-1°; CH2CMe2NMe2, 112°/0.7, 128-9°; CH2CMe2CH2NEt2, 134°/0.3, 138-9°; CH2CH2Y, 140°/0.5, 110-12° (citrate); (CH2)3Y, 148°/0.5, 135-6°; CH2CH2X, 155°/0.3, 179-80°; (CH2)3X, 158°/0.7, 113-15°; b, 130°/0.1, 190-1°; CH2CH2Q, 162°/0.5, 168-9°; CH2CHMeQ, 144°/0.1. 112-14°; 3-(4-methyl-1-piperazinyl) Pr, 190°/0.2, 198-202° (di-HCl salt); c, 170°/0.5, 185°. Also prepared were VIII (n = 0) [R1, R2, b.p./mm. (R3 = Et), m.p. (R3 = H), R3, b.p./mm. of R3, and m.p. of HCl (or citrate) salt given]: Ph, CH2CH2CHMe2, 120°/1.4, -, Z, 145°/0.4, 96-7° (citrate); Ph, Pr, 90°/0.4, -, Z, 126°/0.3, 63-5° (citrate) (CH2CH2Q, 154°/0.4, 104-5°); Ph, tert-Bu, 120°/1, 102-4°, Z, 130°/0.3, 192-3°; Ph, nortricyclyl, 128°/0.1, 119-21°, Z, 170°/0.3, 125-7° (citrate), [CH2CH2Y, 180°/0.4,89-90° (citrate), CH2CH2Q, 190°/0.4, 155-6°]; 4-MeC6H4, iso-Pr, 98°/0.2, 158°, Z, 144°/0.2, 199°; 4-MeOC6H4, iso-Pr, 116°/0.1, 137°, Z, 150°/0.1, 162°, [(CH2)3NMe2, 160°/0.1, 163-4°]; 3-ClC6H4, iso-Pr, 120°/1, 105-7°, z172°/0.4, 159-61° [(CH2)3NMe2, 156°/0.5, 143-5°]; 3-F3CC6H4. iso-Pr, 88°/0.5, -, (CH2)3NMe2, 136°/0.5, 138-40° (Z, 132°/0.5, 154-5°); Ph, Ph,-, -, c, -, 194-5°; 4-MeC6H4, H, 94°/0.5, 143-4°, Z, 140°/0.5, 79-80° (citrate); 4-MeOC6H4, H, 118°/0.3, -, Z, 160°/0.1, 89-90° (citrate). Similarly prepared were R1CO1R2 [R1, b.p./mm. R2 = Et, m.p. R2 = H, R2, b.p./mm. R2, m.p. R2 citrate (or HCl) salt giving]: Ph(iso-Pr)(OH)CCHMe, 118°/0.3, -, Z, 139°/0.5, 105-6°; PhEt(HO)CCHMe, 115°/0.3,-, Z, 146°/0.5, 98-100°; PhEt(HO)CCMe2, -, -, Z, 170°/8, 87-8°; Ph(isoPr)(HO)CCH2CH:CH, -, -, Z, 190°/0.8, 75-6°; 1-hydroxy-2-methylindanyl, -, -, Z, 158°/0.5, 73°; 9-hydroxy-9-fluorenylmethyl, -, 112°, Z, 215°/0.5, 168-9° (HCl salt); 4-ClC6H4OCH2, -, -, CH2CH2NMe2, 140°/0.5, 131° (HCl salt); 6-benzoylbicyclo[2.2.1]-5-hepten-2-yl, -, 130-2°, CH2CH2NMe2, 190°/0.4, 79-80° (HCl salt); 1,2-dimethyl-4-benzoyl-3-cyclohexen-1-yl, -, 137°, Z, 180°/0.2. 170-2° (HCl); 6-(α-hydroxybenzyl)bicyclo[2.2.1]-5-hepten-2-yl, -, 161°, Z, 190°/0.2, 118-20°; 1,4,10,11-tetrahydro-11-fluorenyl, 116°/0.2, 115-16°, Z, 180°/0.1, 135-6°; 1,4-methano-1,4,10,11-tetrahydro-11-fluorenyl, 120°/0.5, 167-8°, Z, 170°/0.2, 129-31°. The Grignard reagent from 18 g. Mg and 79 g. Me2N(CH2)3Cl in 300 mL. THF was added to 89 g. IX in 700 mL. Et2O to give 87.1 g. Ph(HO)(CO2Et)C(CH2)3NMe2, b0.1 130°; HCl salt m. 124°. Similarly prepared were Ph(iso-Pr)CR1R2 (X)(R1 = OH), [R2, b.p./mm., m.p. HCl (or citrate) salt given]: Z, 105°/0.5, 150; CHMeCH2NMe2, 95°/0.5, 210-12°; CH2Z, 124°/0.6, 114-15° (citrate); CH2CH2X (XI), 125/0.6° 160°. A solution of 15 g. VII in 60 mL. Ac2O was treated with 200 mL. AcCl and the mixture kept 2 h. at 30° and evaporated to give 13 g.X(R1 =OAc, R2 = CH2Z), m. 165-6° (AcOEt). Similarly were prepared X. (R1 = OAc) (R2, b.p./mm., and m.p. HCl salt given): Z, 130°/0.5, 82°; CH2CH2X, 136°/0.5, 177-8°; CH2CH2Y, 156°/0.8, 156°; CHMeCH2NMe2, 128°/0.3, 208°. A mixture of 29 g. XI and 8 g. EtCN in 30 mL. AcOH was treated dropwise at 50-60° with a mixture of 60 g. concentrated H2SO4 and 30 mL. AcOH, kept 3 h. at 60°, cooled, poured into aqueous NaOH, and extracted with Et2O to give 21 g. X (R1 = EtCONH, R2 = CH2CH2X), b0.3 180°; HCl salt m. 199-203°. Similarly prepared were X (R1 = HCONH, R2 = CHMeCH2NMe2), b0.3 165°, and X (R1 = HCONH, R2 = CH2CH2X), b0.3 175°. A dispersion of 25 g. Na in 400 mL. PhMe was treated at 20-30° with 56 g. PhCl and 49 g. Et2CHCN. The mixture was treated at 40° with 82.4 g. Ph(iso-Pr)CHCO2Et, kept 2 h. at 40°, treated at 10-20° with 132 g. ClCH2CH2X, and refluxed 4

h. to give 16 g. X (R1 = CO2Et, R2 = CH2CH2X), b0.3 160°; HCl salt m. 135°.

L15 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1964:404161 CAPLUS
DOCUMENT NUMBER: 61:4161
ORIGINAL REFERENCE NO.: 61:634e-h,635a-e
TITLE: Hydroxy β-lactones from 3,4-epoxycarboxylic acids
AUTHOR(S): Falbe, Juergen; Schulze-Steinen, Hans Juergen; Korte, Friedhelm
CORPORATE SOURCE: Shell Grundlagenforschung G.m.b.H., Schloss Birlinghofen and Siegburg, Germany
SOURCE: Ber. (**1964**), 97(4), 1096-1103
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 61:4161
GI For diagram(s), see printed CA Issue.
AB 3,4-Epoxycarboxylic acids can be rearranged in acidic medium to hydroxy β-lactones. This reaction can also be applied to epoxy lactones. However, 3,4-epoxycarboxylic acid esters were rearranged under the same conditions to β-hydroxy γ-lactones. CH2:CMeCMe2CO2H (I) (60 g.) in 100 cc. CH2Cl2 treated with 2.5 g. AcONa and then with stirring during 1.5 hrs. with 100 g. 40% AcOOH at 15-20° and the mixture stirred about 20 hrs. at room temperature yielded 57 g. II, m. 66° (AcOEt). Similarly were prepared the following III (R, R', g.-yield, m.p., and starting material and g.-amount used given): H, H, 55, 117-18° (AcOEt), **cyclohexene**-1-**carboxylic acid** (IV), 70; H, Me, 88, 106° (AcOEt), 2-(1-cyclohexenyl)**propionic acid** (V), 154; Me, Me (VI), 35.0, 56° (AcOEt), 2-(1-cyclohexenyl)isobutyric acid (VII), 33.6. EtCH:CHCH2CO2H (57 g.) epoxidized yielded 65 g. oily 3,4-epoxy derivative (VIII). Crude VIII (15 g.) in 50 cc. 3% H2SO4 stirred 18 hrs. at room temperature yielded IX (R = R' = H, R'' = Et), Rf 0.81, and X (R = R' = H, R'' = Et), Rf 0.66. CH2:CHCMe2CO2H (21 g.) epoxidized in the usual manner gave 17.9 g. IX (R = R' = Me, R'' = Et), Rf 0.96, and X (R = R' = Me, R'' = Et), Rf 0.88. 4,4-Dimethyl-6,7,8,8a-tetrahydro-3H-2-benzopyran-3-one (27 g.) epoxidized during 20 hrs. with AcOOH gave 29 g. crystalline 4α,5-epoxy-4,4-dimethylperhydro-2-benzopyran-3-one (XI), m. 89.5° (AcOEt-petr. ether). XI (7 g.), 700 cc. H2O, and 1 cc. concentrated H2SO4 stirred 18 hrs. at room temperature gave 4.7 g. crystalline XII, m. 151° (1:1 AcOEt-petr. ether). II (10 g.) and 80 g. 10% aqueous KOH stirred 2 hrs. at 50°, cooled, and acidified to pH 3 with dilute HCl yielded 8.6 g. XIII, m. 103-6° (Et2O). V. (10 g.) and 60 g. 10% aqueous KOH gave similarly 8.8 g. XIV, mI 151° (Et2O). XII (300 mg.) and 10 cc. 0.1N NaOH stirred 1 hr. at 40° and 0.5 hr. at 90° gave a mixture of XV and XVI. Et **ester** (78 g.) of I epoxidized yielded 50 g. 3,4-epoxide (XVII), b11 78-81°, and 16 g. XIII, b0.07-0.1 73-88°, m. 99° (ligroine, b. 40-80°), 105-6° (Et2O). Similarly were prepared 20.5 g. epoxide from 25 g. tert-Bu **ester** (XVIII) of I; 58 g. crude 3,4-epoxy derivative (XIX) from 60 g. Et **ester** of CH2:CHCMe2CO2H [the product contained some X (R = R' = Me, R'' = H) (XX)]; 37g. XXI (R = R' = H, R'' = Et) (XXII), b0.6 73-4°, b0.25 67°, from 42 g. IV; 69 g. XXI (R = H, R' = Me, R'' = Et) (XXIII), b0.6 50-1°, from 91 g. V; 77.3 g. XXI (R = R' = Me, R'' = Et) (XXIV), b10 119°, from 78.5 g. VII; 21.4 g. XXI (R = R' = Me, R'' = tert-Bu) (XXV), m. 45.5-6.5° (ligroine). XVII (20.0 g.) and 100 cc. 3% H2SO4 stirred 3 days at room temperature gave 7.5 g. XIII, b0.2 100-8°, m. 105-6° (Et2O), which was also obtained similarly from XVIII. XIX (10 g.) in 50 cc. 3% H2SO4 stirred 40 hrs. at room temperature gave 7 g. crude XX. XIX (10 g.) in 50 cc. 3% H2SO4-Et2O stirred 24 hrs. at 40° gave 8.1 g. crude XIX, which redistd. yielded pure XIX, b0.05 81°. XXII (20 g.) in 100 cc. 3% H2SO4 stirred 3 days at room temperature yielded 8 g. XXVI (R = R' = H), b0.6 138°. XXIII (15.0 g.) in 50 cc 3% H2SO4 gave similarly during 40 hrs. 6.0 g. XXVI (R = H, R' = Me), b0.5 106°, m. 32% and an unsatd. γ-lactone (2.7 g.), b0.1 83°, containing 1 mole H2O less than XXVI (R = H, R' = Me). XXV (20.0 g.) and 400 cc. 3% H2SO4 stirred 3 days at room temperature and 1 day at 60° gave 13.7 g. XXVI (R = R' = Me), m. 150.5-1.5° (Et2O), which was also obtained similarly from XXIV.

C:\STNEXP4\QUERIES\383.str





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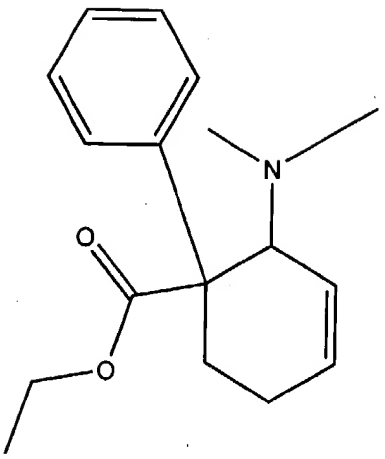
21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15
ring/chain nodes :
7 8 9 16 17 18 19 20
chain bonds :
3-41 4-42 5-39 5-40 6-37 6-38 11-25 12-24 13-23 14-21 15-22 17-29 17-30 17-31
18-26 18-27 18-28 19-32 19-33 20-34 20-35 20-36
ring/chain bonds :
1-7 1-10 2-16 7-8 7-9 9-19 16-17 16-18 19-20
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
1-7 1-10 19-20
exact bonds :
1-2 1-6 2-3 2-16 3-4 3-41 4-5 4-42 5-6 5-39 5-40 6-37 6-38 7-8 7-9 9-19
11-25 12-24 13-23 14-21 15-22 16-17 16-18 17-29 17-30 17-31 18-26 18-27 18-28
19-32 19-33 20-34 20-35 20-36
normalized bonds :
10-11 10-15 11-12 12-13 13-14 14-15

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS
39:CLASS 40:CLASS 41:CLASS 42:CLASS



ethyl 2-dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate

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=> s l16 full
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.



FULL SEARCH INITIATED 14:54:56 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  34224 TO ITERATE

100.0% PROCESSED   34224 ITERATIONS                              33 ANSWERS
SEARCH TIME: 00.00.01

L17          33 SEA SSS FUL L16



L18        234 L17

=> s l18 and ethyl and ester
        419257 ETHYL
        552789 ESTER
L19           8 L18 AND ETHYL AND ESTER

=> d 1-8 ibib abs hitstr

L19  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:367260  CAPLUS
DOCUMENT NUMBER:          140:380641
TITLE:                    Solid drug delivery systems for opiates, opioids and
                          stimulants that are protected against abuse using
                          antagonists
INVENTOR(S):              Bartholomaeus, Johannes; Langner, Klaus-Dieter
PATENT ASSIGNEE(S):       Gruenenthal GmbH, Germany
SOURCE:                   Ger. Offen., 15 pp.
                          CODEN: GWXXBX
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     DE 10250088           A1    20040506    DE 2002-10250088        20021025
     WO 2004037260         A1    20040506    WO 2003-EP11785         20031024
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                          DE 2002-10250088    A  20021025
AB    The invention concerns two-compartment solid drug delivery systems for
      opiates, opioids and stimulants in order to prevent drug abuse; one
      compartment includes the drug the other compartment contains an antagonist
      or antagonists to the drug.  When drugs are used for medical purpose, the
      antagonist is not dissolved.  In case the formulation is disintegrated,
      and/or extracted for drug overuse, the antagonists are in the same phase as
      the drug for action.  Layered tablets can be produced; or identical, but
      not labeled tablets, pellets are prepared from drug and antagonist.  Thus a
      two layer tablet contained (mg): in the coating: naltrexone hydrochloride
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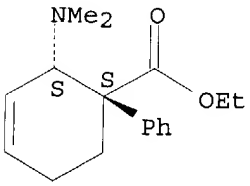
50; Cutina HR 50; in the outer layer: morphine sulfate pentahydrate 60; methylhydroxy Pr cellulose 100; microcryst. cellulose 165; lactose monohydrate 165; magnesium stearate 5; silica 5.

IT **20380-56-7**, 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, **ethyl ester**, (1R,2R)-rel- **51931-66-9**
, 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, **ethyl ester**, (1R,2S)-rel-
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid drug delivery systems for opiates, opioids and stimulants that are protected against abuse using antagonists)

RN 20380-56-7 CAPLUS

CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, (1R,2R)-rel- (9CI) (CA INDEX NAME)

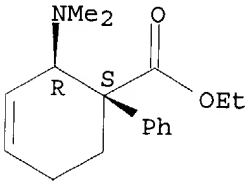
Relative stereochemistry.



RN 51931-66-9 CAPLUS

CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:5117 CAPLUS

DOCUMENT NUMBER: 140:47586

TITLE: Solid, delayed-release pharmaceutical composition comprising tilidine hydrochloride

INVENTOR(S): Schumann, Christof; Renz, Jessica

PATENT ASSIGNEE(S): Stada Arzneimittel A.-G., Germany

SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1374859	A1	20040102	EP 2003-14715	20030627

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: DE 2002-10229216 A 20020628

AB The invention concerns a solid, stable formulation of tilidine hydrochloride hemihydrate that contains retarding agents, excipients, but no agents that would form complexes with two-and three-valent metals and pyrazole acetic acid. Addnl. the morphine antagonist naloxone can be included into the formulations. Thus a tablet contained (mg/tablet):

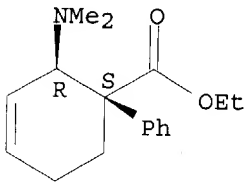
tilidine hydrochloride x 0.5 102.9; naloxone hydrochloride dihydrate 8.8; hydroxypropylmethyl cellulose (4000 cP) 55; hydroxypropyl methylcellulose (100 cP) 35; microcryst. cellulose 149 mg; silica 3; magnesium stearate 2. The tablets were coated with Opadry.

IT **27107-79-5**, Tilidine hydrochloride
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid, delayed-release pharmaceutical composition comprising tilidine hydrochloride)

RN 27107-79-5 CAPLUS

CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, hydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



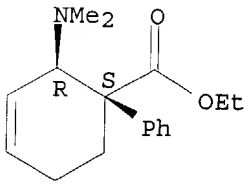
● HCl

IT **255733-17-6**, 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, **ethyl ester**, hydrochloride, hydrate (2:1), (1R,2S)-rel-
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(solid, delayed-release pharmaceutical composition comprising tilidine hydrochloride)

RN 255733-17-6 CAPLUS

CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, hydrochloride, hydrate (2:1), (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

● 1/2 H_2O

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1006739 CAPLUS
DOCUMENT NUMBER: 140:47524
TITLE: Drug delivery systems with abuse-protection for tranquilizers, hypnotics, sedatives and stimulants containing thickening agents

INVENTOR(S): Bartholomaeus, Johannes; Kugelmann, Heinrich
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

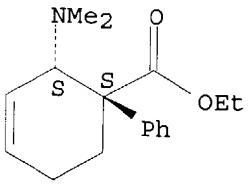
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105808	A1	20031224	WO 2003-EP6314	20030616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10250083	A1	20031224	DE 2002-10250083	20021025
PRIORITY APPLN. INFO.:			DE 2002-10227077 A	20020617
			DE 2002-10250083 A	20021025

AB The invention relates to a solid administration form, protected from parenteral abuse and containing at least one viscosity-increasing agent in addition to one or more active substances that have parenteral abuse potential. Said agent forms, when a necessary min. amount of an aqueous liquid is added, on the basis of an extract obtained from the administration form, a preferably injectable gel that remains visually distinct when introduced into another quantity of an aqueous liquid Thus a matrix tablet contained (mg): (-)-(1R,2R)-3-(3-dimethylamino-1-**ethyl**-2-methyl-propyl)phenol hydrochloride 100; hydroxypropyl methylcellulose 70; Xanthan 10; cellulose 123; silica 4; magnesium stearate 3.

IT **20380-56-7**, 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, **ethyl ester**, (1R,2R)-rel- **51931-66-9**, 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, **ethyl ester**, (1R,2S)-rel-
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems with abuse-protection for tranquilizers, hypnotics, sedatives and stimulants containing thickening agents)

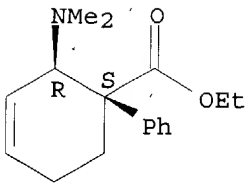
RN 20380-56-7 CAPLUS
CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 51931-66-9 CAPLUS
CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:513662 CAPLUS
DOCUMENT NUMBER: 133:89330
TITLE: Reduction of **ethyl** 3-dimethylamino-2-phenylpropionate content in solutions of **ethyl** 2-dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate using carboxylic acids.
INVENTOR(S): Thyes, Marco; Falkenberg, Wolfgang; Schneider, Ulrich
PATENT ASSIGNEE(S): Knoll Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043353	A1	20000727	WO 2000-EP306	20000115
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19902590	A1	20000727	DE 1999-19902590	19990122
TW 462958	B	20011111	TW 1999-88122113	19991216
CA 2359080	AA	20000727	CA 2000-2359080	20000115
BR 2000007646	A	20011016	BR 2000-7646	20000115
EP 1144361	A1	20011017	EP 2000-902598	20000115
EP 1144361	B1	20040818		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002535303	T2	20021022	JP 2000-594771	20000115
RU 2201918	C1	20030410	RU 2001-123589	20000115
AU 766196	B2	20031009	AU 2000-24376	20000115
ZA 2001005537	A	20020705	ZA 2001-5537	20010705
NO 2001003528	A	20010717	NO 2001-3528	20010717

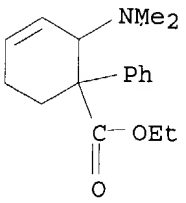
PRIORITY APPLN. INFO.:
DE 1999-19902590 A 19990122
WO 2000-EP306 W 20000115

AB The amount of Et 3-dimethylamino-2-phenylpropionate (I) impurity in a solution of Et 2-dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate (II) in a non-H2O miscible solvent is reduced by treatment with 0.5-2.0 equiv of carboxylic acid per mol II followed by stirring at 50-100°. Thus, II containing 1% I in cyclohexane was refluxed 2 h with HOAc; the mixture was treated with H2O and aqueous NaOH followed by phase separation to give II containing 0.05% I.

IT **17243-69-5P**
RL: PUR (Purification or recovery); PREP (Preparation)
(reduction of Et 3-dimethylamino-2-phenylpropionate content in solns. of Et 2-dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate using carboxylic acids)

RN 17243-69-5 CAPLUS
CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester

(8CI, 9CI) (CA INDEX NAME)

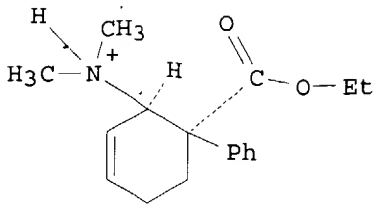


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

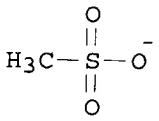
L19 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:708727 CAPLUS
DOCUMENT NUMBER: 131:310449
TITLE: Preparation of the analgesic tilidine mesylate
INVENTOR(S): Shickaneder, Helmut; Nikolopoulos, Aggelos; Bruton, Brian
PATENT ASSIGNEE(S): Russinsky Ltd., Ire.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9955662	A1	19991104	WO 1999-IE24		19990409
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DE, DK, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9934402	A1	19991116	AU 1999-34402		19990409
AU 744888	B2	20020307			
EP 1073625	A1	20010207	EP 1999-916009		19990409
EP 1073625	B1	20030611			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
DE 19981795	T	20010510	DE 1999-19981795		19990409
AT 242760	E	20030615	AT 1999-916009		19990409
PT 1073625	T	20031128	PT 1999-916009		19990409
ES 2204119	T3	20040416	ES 1999-916009		19990409
ZA 2000001587	A	20001025	ZA 2000-1587		20000329
PRIORITY APPLN. INFO.:			IE 1998-322	A	19980428
			WO 1999-IE24	W	19990409

OTHER SOURCE(S): CASREACT 131:310449
GI



I



AB Tilidine mesylate (I; m.p. 136°), an analgesic which is prepared in high yield by the salification of tilidine with methanesulfonic acid in a solvent (e.g., Et acetate) at 0-80°, has increased stability, a less bitter taste, and an increased pH range in aqueous solns. over which it's stable in comparison to known tilidine salts. Pharmaceutical dosage forms containing I are presented and claimed.

IT **247248-28-8P**
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of the analgesic tilidine mesylate)

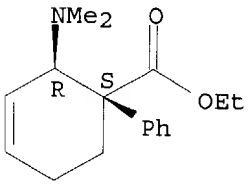
RN 247248-28-8 CAPLUS

CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, (1R,2S)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

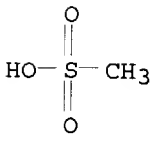
CRN 51931-66-9
CMF C17 H23 N O2

Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

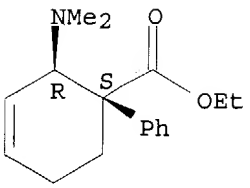


IT **51931-66-9**, Tilidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of the analgesic tilidine mesylate)

RN 51931-66-9 CAPLUS

CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, (1R,2S)-rel- (9CI) (CA INDEX NAME)

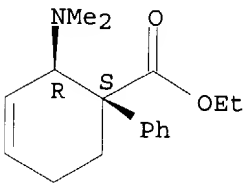
Relative stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:399268 CAPLUS
DOCUMENT NUMBER: 131:210159
TITLE: Thin-layer chromatography and mass spectrometry for screening of biological samples for drugs and metabolites
AUTHOR(S): Brzezinka, Harald; Dallakian, Pavel; Budzikiewicz, Herbert
CORPORATE SOURCE: Institut fur Rechtsmedizin der Universitat Bonn, Bonn, 53111, Germany
SOURCE: Journal of Planar Chromatography--Modern TLC (1999), 12(2), 96-108
CODEN: JPCTE5; ISSN: 0933-4173
PUBLISHER: Research Institute for Medicinal Plants
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper describes a method for off-line coupling of thin-layer chromatog. (TLC) and electron-impact ionization mass spectrometry (EIMS) which is well suited for routine forensic and toxicol. investigations of a large number of samples. The advantages and drawbacks of this approach are discussed. Several TLC systems for 493 compds. of forensic and toxicol. interest are described and eight-peak mass spectra from full EI mass spectra are listed.
IT **51931-66-9**, Tilidine
RL: ANT (Analyte); ANST (Analytical study)
(thin-layer chromatog. and mass spectrometry for screening of biol. samples for drugs and metabolites)
RN 51931-66-9 CAPLUS
CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, (1R,2S)-rel- (9CI) (CA INDEX NAME)

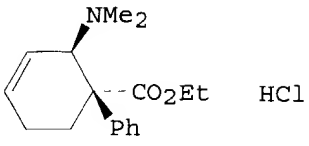
Relative stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:593563 CAPLUS
DOCUMENT NUMBER: 87:193563
TITLE: Metabolism of trans-D,L-2-(dimethylamino)-1-phenyl-3-cyclohexene-1-carboxylic acid **ethyl ester** hydrochloride (tilidine-HCl). Part 3. Renal metabolite elimination in rats, dog, and man
AUTHOR(S): Vollmer, K. O.; Von Hodenberg, A.
CORPORATE SOURCE: Forschungsinst., Goedecke A.-G., Freiburg/Br., Fed. Rep. Ger.
SOURCE: Arzneimittel-Forschung (1977), 27(9), 1706-13

CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



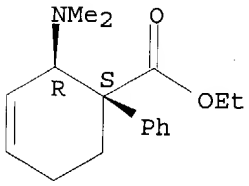
I

AB Renal elimination of tilidine-HCl (I) [**27107-79-5**] was similar in the rat, dog, and man. After oral administration of I-14C 50-60, 80, and >90% of the applied dose was eliminated in the urine in the resp. species. The half/life of renal 14C elimination was 8 h in the rat and man, and the elimination was faster in the dog. In all species, about 17% of the urinary radioactivity was in nonpolar metabolites. About 2-3% each was in nortilidine [38677-94-0] and bisnortilidine [53948-51-9], and <0.2% in unchanged I. Most of the polar metabolites were glucuronides. Five new metabolites, oxygenated derivs. of nortilidine and bisnortilidine, were isolated from rat urine.

IT **27107-79-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of)

RN 27107-79-5 CAPLUS
CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, hydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

L19 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1973:3822 CAPLUS
DOCUMENT NUMBER: 78:3822
TITLE: **Ethyl** 4-amino-1-phenyl-2-cyclohexene-1-carboxylates
INVENTOR(S): Satzinger, Gerhard; Herrmann, Manfred
PATENT ASSIGNEE(S): Goedecke A.-G.
SOURCE: Ger. Offen., 42 pp. Division of Ger. Offen. 2,107,871.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2166019	A	19720831	DE 1971-2166019	19710218
DE 2166019	B2	19750612		
DE 2166019	C3	19760212		

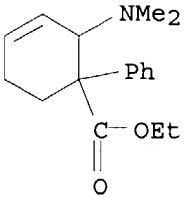
PRIORITY APPLN. INFO.: DE 1971-2166019 19710218
GI For diagram(s), see printed CA Issue.

AB Twenty-eight Et cyclohexenecarboxylates [I; R = H, Me, Et, Bu; R1 = H, Me, Et, Bu, allyl, phenylalkyl, etc.; NRR1 = morpholino, substituted piperazinyl, substituted piperidino] and (or) their salts useful as analgesics, antipyretics, sedatives, etc., were prepared from the cyclohexene (II; R4 = OAc). II (R4 = OAc) was hydrolyzed and then halogenated to give II (R4 = halo), which was treated with R1NHR to give I. II (R4 = OAc) was prepared by treating Et atropate with MeCH:CCHO-Ac2O.

IT **17243-69-5P 24357-97-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

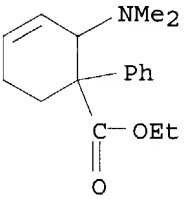
RN 17243-69-5 CAPLUS

CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester (8CI, 9CI) (CA INDEX NAME)



RN 24357-97-9 CAPLUS

CN 3-Cyclohexene-1-carboxylic acid, 2-(dimethylamino)-1-phenyl-, ethyl ester, hydrochloride (8CI, 9CI) (CA INDEX NAME)



● HCl